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SUBSTITUTE FORM PTO-1390 — U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 06275/188001

U.S. APPLICATION NO (IF KNOWN): 09/367950

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/SE99/01031	June 10, 1999	June 11, 1998

TITLE OF INVENTION
NEW USE

APPLICANT(S) FOR DO/EO/US
TOMMY EKSTRÖM

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ■ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.

2. □ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.

3. □ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

4. □ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. ■ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. □ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ■ has been transmitted by the International Bureau.
   c. □ is not required, as the application was filed in the United States Receiving Office (RO/US).

6. □ A translation of the International Application into English (35 U.S.C. 371(c)(2)).

7. ■ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. □ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. □ have been transmitted by the International Bureau.
   c. ■ have not been made; however, the time limit for making such amendments has NOT expired.
   d. □ have not been made and will not be made.

8. □ A translation of amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

9. ■ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).

10. □ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other documents or information included:

11. ■ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.

12. ■ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

13. ■ A FIRST preliminary amendment.
    □ A SECOND or SUBSEQUENT preliminary amendment.

14. □ A substitute specification.

15. □ A change of power of attorney and/or address letter.

16. □ Other items or information:

"Express Mail" mailing label number EL224675189US
Date of Deposit August 18, 1999
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner For Patents, Washington, D.C. 20231

Cony Madera

Cony Madera

514 Rec'd PCT/PTO 18 AUG 1999

U.S. APPLICATION NO. (IF KNOWN)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/367950	PCT/SE99/01031	06275/188001

17. ■ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)):		
Search report has been prepared by the EPO or JPO ..... $ 840		
International preliminary examination fee paid to USPTO (37 CFR 1.482)..... $ 670		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2))..... $ 760		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO..... $ 970		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2) to (4)..... $ 96		
ENTER APPROPRIATE BASIC FEE AMOUNT	$ 970.00	
Surcharge of $130 for furnishing the oath or declaration later than □ 20 □ 30 mos from the earliest claimed priority date (37 CFR 1.492(e)).	$ 0.00	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
TOTAL CLAIMS	12 - 20	0	x $ 18	$ 0.00	
INDEPENDENT CLAIMS	1 - 3	0	x $ 78	$ 0.00	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $260	$ 0.00	
TOTAL OF ABOVE CALCULATIONS				$ 970.00	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28.)				$ 0.00	
SUBTOTAL				$ 970.00	
Processing fee of $130 for furnishing the English Translation later than □ 20 □ 30 mos. from the earliest claimed priority date (37 CFR 1.492(f))				$ 0.00	
TOTAL NATIONAL FEE				$ 970.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31).				$ 40.00	
TOTAL FEES ENCLOSED				$1,010.00	
				Amount to be refunded	
				Charged	

a. ■ A check in the amount of $1,010.00 to cover the above fees is enclosed.
b. □ Please charge my Deposit Account No. 06-1050 in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.
c. ■ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-1050. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

JANIS K. FRASER, Ph.D., J.D.
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SIGNATURE

Janis K. Fraser, Ph.D., J.D.
NAME

34,819
REGISTRATION NUMBER

PATENT
ATTORNEY DOCKET NO. 06275/188001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Tommy Ekström
Serial No.:
Filed : HEREWITH
Title : NEW USE

Art Unit:
Examiner:

Internat'l Appln. No.: PCT/SE99/01031
Internat'l Filing Date: June 10, 1999

Box PCT

Assistant Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the Claims:

Cancel claims 1-12.

In claim 15, line 1, delete "or 14".

In claim 16, line 1, delete "any one of claims 13 to 15" and insert --claim 13--.

In claim 17, line 1, delete "any one of claims 13 to 16" and insert --claim 13--.

In claim 18, line 1, delete "any one of claims 13 to 17" and insert --claim 13--.

In claim 19, line 1, delete "any one of claims 13 to 18" and insert --claim 13--.

In claim 20, line 1, delete "any one of claims 13 to 19" and insert --claim 13--.

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Date of Deposit August 18, 1999

I hereby certify under 37 CFR 1.10 that this correspondence is being deposited with the United States Postal Service as **"Express Mail Post Office To Addressee"** with sufficient postage on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Cory Madera

Cory Madera

In claim 21, line 1, delete "any one of claims 13 to 20" and insert --claim 13--.

In claim 22, line 1, delete "any one of claims 13 to 21" and insert --claim 13--.

In claim 23, line 1, delete "any one of claims 13 to 22" and insert --claim 13--.

REMARKS

Claims 13-24 are now pending in the application, claims 1-12 having been cancelled. Claims 15-23 are amended to remove multiple dependency. No new matter has been added.

Respectfully submitted,

Date: Aug. 18, 1999

Janis K. Fraser, Ph.D., J.D.
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390337.B11

NEW USE

FIELD OF THE INVENTION

The present invention relates to use of a composition for symptomatic relief, when needed, comprising, in admixture

(a) a first active ingredient which is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and

(b) a second active ingredient which is budesonide;

for the manufacture of a medicament for use in the prevention or treatment of an acute condition of asthma and/or intermittent asthma and/or episodes in chronic asthma. The invention further relates to a method for prevention or treatment of an acute condition of asthma and/or intermittent asthma and/or episodes in chronic asthma by administering, by inhalation, a composition comprising the first and second active ingredients as defined previously.

BACKGROUND OF THE INVENTION

Despite recent advances in the awareness of asthma and the introduction of powerful and effective anti-asthma drugs, asthma remains a poorly understood and frequently poorly treated disease. There have been recent advances in the treatment of the disease which result from the recognition that asthma is a chronic inflammatory disease. Therapy is now aimed at both controlling the symptoms and reducing the inflammation. The symptoms may be controlled by β_2-adrenoceptor agonists such as terbutaline, salbutamol, formoterol and salmeterol. Prophylactic therapy is typically provided by steroids such as beclomethasone dipropionate, fluticasone propionate, mometasone furoate and budesonide.

In spite of modern maintenance treatment too many asthmatic patients are undertreated for a number of reasons with a negative impact on their quality of life. Too complicated therapy with different medications and devices may lead to misunderstanding and commu-

nication problems between patient and doctor. Poor compliance is a common phenomenon. Improved patient education may partly counteract this, but does not completely solve the problem. A new and more simple approach to asthma treatment could thus be of tremendous help for many patients suffering from respiratory disease, particularly asthma. The combination of budesonide and formoterol in the same device as suggested in PCT applications WO 93/11773 and WO 98/15280 (both to Astra AB of Sweden) offers a favorable pathway to improve today's asthma management with an excellent safety profile. However, although having an adequate regular, e.g. bid. treatment with such a combination, many patients will now and then run into acute situations with a higher frequency and severity of exacerbations, when additional medication is needed. Such an additional medication is often a β_2-adrenoceptor agonist with fast onset, normally terbutaline or salbutamol. A second medicament is thus needed, and this can negatively affect the overall compliance of the patient. There is thus need for a neat way of handling maintenance treatment together with the treatment of acute situations which .

SUMMARY OF THE INVENTION

It is an object of the present invention to provide use of a suitable composition for the manufacture of a medicament for the treatment of acute episodes of asthma as a complement to maintenance treatment.

More specifically, according to the invention there is provided use of a composition for symptomatic relief when needed comprising, in admixture

(a) a first active ingredient which is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and

(b) a second active ingredient which is budesonide;

for the manufacture of a medicament for use in the prevention or treatment of an acute condition of asthma and/or intermittent asthma and/or episodes in chronic asthma.

Use of the present composition, when needed, relates to use of said composition during one or more of the following conditions:

i) an acute condition of asthma, i.e. acute asthma attacks,

ii) intermittent asthma and/or

iii) short periods (episodes) of acute attacks of bronchospasms in chronic asthma.

Acute asthma attacks may occur on an irregular basis when exposed to an agent e.g. during the pollen season, a virus infection, cold air, perfumes or any other agent(s) triggering an asthma attack in the patient.

It lies within the scope of the present invention, to use the compositions comprising active compounds (a) and (b) for treating acute conditions of asthma, intermittent asthma and episodes in chronic asthma, in addition to treating chronic asthma on a regular basis, with the same active compounds (a) and (b) or one or more different active compounds, preferably selected from short-acting β-agonists, long-acting β-agonists and glucocorticosteroids.

We contemplate preventive use when the patient expects to encounter asthma inducing conditions e.g. intends to take exercise or go into smoky conditions.

According to a further aspect of the invention a method of prevention or treatment of an acute condition of asthma and/or intermittent asthma and/or episodes in chronic asthma, when needed, which comprises administering, by inhalation, to a patient an effective amount of a composition comprising, in admixture:

(a) a first active ingredient which is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and

(b) a second active ingredient which is budesonide.

According to the present invention it has surprisingly been found that the medicament can be administered when needed to a patient with an acute attack of asthma.

The recommended dose regimen described in the prior art as disclosed above is twice a day. This dose recommendation was a result of a concern not to have too high an administration of the active compounds. However, in the present invention it has been found that it is possible for the patient to administer this mixture as often as needed.

The combination of formoterol and budesonide can be used as a rescue medication. Worsening of symptoms can be counteracted by incremental use of the combination for symptom relief, e.g. during exacerbations with the additional steroid component coming in as early as possible to suppress the enhanced airway inflammation. The long duration of formoterol will reduce the risk of too frequent dosing. When taking the combination budesonide/formoterol when needed the severity of exacerbations can be reduced. The as needed use (Pro Re Nata, PRN) will also minimize the difficulty of predicting which patients will be controlled on a low dose of inhaled steroid rather than increasing the steroid dose before adding a long-acting β_2-agonist. Under-treatment with inhaled glucocorticosteroids following a too low maintenance dose will be more or less "self-corrected" by the rescue usage according to the present invention. The PRN use of the combination will always give some beneficial anti-inflammatory effects even if it is used by the patient only for rescue purposes. A treatment for patients suffering from respiratory disease, particularly asthma (including allergic conditions, e.g. episodic or intermittent asthma), will therefore be to use the combination formoterol/budesonide for maintenance therapy as well as on an as needed basis (for rescue purposes), e.g. for prevention of exercise and/or allergen induced asthma.

DETAILED DESCRIPTION OF THE INVENTION

Formoterol is a compound which can exist in several stereochemical forms. The present invention includes the individual stereoisomers as well as mixtures thereof. It is intended that the present invention includes geometrical isomers, rotational isomers, racemates, diastereomers and enantiomers, in particular the R,R enantiomer of formoterol.

Suitable physiologically salts of formoterol include acid addition salts derived from inorganic and organic acids such as the hydrochloride, hydrobromide, sulfate, phosphate, maleate, fumarate, tartrate, citrate, benzoate, 4-methoxybenzoate, 2- or 4-hydroxybenzoate, 4-chlorobenzoate, p-toluenesulphonate, methanesulphonate, ascorbate, salicylate, acetate, succinate, lactate, glutarate, gluconate, tricarballylate, hydroxy-naphthalene-carboxylate or oleate. Formoterol is preferably used in the form of its fumarate salt and as a dihydrate of this salt.

The present invention also encompasses compositions comprising the 22R epimer of budesonide as the second active ingredient.

A suitable unit dose of formoterol (as fumarate dihydrate) is in the range of from 1 µg to 48 µg, preferably from 2 µg to 24 µg, and more preferably between 3 µg and 12 µg. The daily dose of formoterol (as fumarate dihydrate), including maintenance therapy, should be in the range of from 1 µg to 100 µg, preferably from 2 µg to 60 µg, and more preferably from 3 µg to of 48 µg.

A suitable unit dose of budesonide is in the range of from 20 µg to 1600 µg, suitably from 30 µg to 800 µg, preferably from 50 µg to 400 µg, and more preferably between 100 µg and 200 µg. The daily dose of budesonide, including maintenance therapy, should be in the range of 20 µg to 4800 µg, preferably from 30 µg to 3200 µg, and more preferably from 40 µg to 1600 µg. The particular dose regimen will depend on the patient (age, sex, weight etc.) and the severity of the disease (mild, moderate, severe asthma etc.).

The molar ratio of the first active ingredient (as formoterol) to the second active ingredient of the invention, suitably lies in the range of from 1:1 to 1:100, preferably from 1:1 to 1:70, and more preferably from 1:1 to 1:50.

Preferably the mixture comprises one or more pharmaceutically acceptable additives, diluents or carriers, more preferably in an amount of from 50 μg to 4000 μg in each dose, most preferably in an amount of from 100 μg to 2000 μg and most preferably from 100 μg to 1000 μg. Examples of suitable additives, diluents or carriers include lactose, dextran, mannitol or glucose. Preferably lactose is used, and more preferably as the monohydrate.

One or more of the ingredients of the mixture may be in the form of dry powder, more preferably a small particle dry powder, most preferably an agglomerated small particle dry powder. Alternatively one or more of the active ingredients (a) or (b) are in the form of an ordered mixture with diluent, additive or carrier. The ingredients used in the invention can be obtained in these preferred forms using methods known to those skilled in the art. The particle size of the active ingredients is preferably less than 10 μm.

Administration may be by inhalation orally or intranasally. The ingredients of the system are preferably adapted to be administered from a dry powder inhaler, a pressurized metered dose inhaler, or a nebulizer.

When the ingredients of the system are adapted to be administered from a pressurized inhaler, they are preferably in a small particle form. They are dissolved, or, preferably, suspended in a liquid propellant mixture. The propellants which can be used include chlorofluorocarbons, hydrocarbons or hydrofluorocarbons. Especially preferred propellants are P134a (tetrafluoroethane), P152a (difluoroethane) and P227 (heptafluropropane) each of which may be used alone or in combination. They are optionally used in combination with one or more other propellants and/or one or more surfactants and/or one or more other excipients, for example ethanol, a lubricant, an antioxidant and/or a stabilizing agent.

When the ingredients of the system of the invention are adapted to be administered via a nebulizer they may be in the form of a nebulized aqueous suspension or solution, with or without suitable pH or tonicity adjustment, either as a unit dose or multidose formulation.

EXAMPLES

The ingredients can be formulated as illustrated by the following examples which are not intended to limit the scope of the invention.

In the examples micronization is carried out in a conventional manner such that the particle size range for each component is suitable for administration by inhalation. Turbuhaler® is a trademark of Astra AB.

EXAMPLE 1

4.5 Parts by weight of formoterol fumarate dihydrate were mixed with 915 parts by weight of lactose monohydrate. The blend was micronized using a high pressure air jet mill and then conditioned using the process of EP-A-717 616. 80 Parts by weight of micronized budesonide were added to the conditioned product by mixing and homogenizing with a low pressure jet mill. The mixture was then spheronized using the process of EP-A-721 331 and filled into the storage compartment of Turbuhaler.®

EXAMPLE 2

9 Parts by weight of formoterol fumarate dihydrate were mixed with 831 parts by weight of lactose monohydrate. The blend was micronized using a high pressure air jet mill and then conditioned using the process of EP-A-717 616. 160 Parts by weight of micronized budesonide were added to the conditioned product by mixing and homogenizing with a low

pressure jet mill. The mixture was then spheronized using the process of EP-A-721 331 and filled into the storage compartment of Turbuhaler.®

EXAMPLE 3

6 Parts by weight of formoterol fumarate dihydrate were mixed with 894 parts by weight of lactose monohydrate. The blend was micronized using a high pressure air jet mill and then conditioned using the process of EP-A-717 616. 100 Parts by weight of micronized budesonide were added to the conditioned product by mixing and homogenizing with a low pressure jet mill. The mixture was then spheronized using the process of EP-A-721 331 and filled into the storage compartment of Turbuhaler.®

EXAMPLE 4

12 Parts by weight of formoterol fumarate dihydrate were mixed with 788 parts by weight of lactose monohydrate. The blend was micronized using a high pressure air jet mill and then conditioned using the process of EP-A-717 616. 200 Parts by weight of micronized budesonide were added to the conditioned product by mixing and homogenizing with a low pressure jet mill. The mixture was then spheronized using the process of EP-A-721 331 and filled into the storage compartment of Turbuhaler.®

EXAMPLE 5

A patient on maintenance treatment with the fixed combination formoterol fumarate dihydrate/budesonide in a dose of 4.5/80 µg or 4.5/160 µg bid additionally uses the same combination either for rescue purposes once or twice daily to treat sporadic breakthrough symptoms, or as needed to treat exacerbations during one or two weeks, with a maximum daily dose of 36/640 µg (8 puffs of 4.5/80 µg) and 36/1280 µg (8 puffs of 4.5/160 µg), respectively.

EXAMPLE 6

A patient with intermittent asthma uses the fixed combination formoterol fumarate dihydrate/budesonide as sole medication to be taken as needed until the asthma resolves. The highest recommended daily dose will be either 36/640 µg (8 puffs of 4.5/80 µg) or 36/1280 µg (8 puffs of 4.5/160 µg) for a period not exceeding 8-120 weeks. If symptoms still persist after that period of time - regular maintenance therapy should be considered.

CLAIMS

1. Use of a composition for symptomatic relief, when needed, comprising, in admixture

(a) a first active ingredient which is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and

(b) a second active ingredient which is budesonide;

for the manufacture of a medicament for use in the prevention or treatment of an acute condition of asthma and/or intermittent asthma and/or episodes in chronic asthma.

2. Use according to claim 1, wherein the molar ratio of (a) to (b) calculated as formoterol to budesonide is from 1:1 to 1:100, preferably from 1:1 to 1:70.

3. Use according to claim 1 or 2, wherein the first active ingredient is formoterol fumarate dihydrate.

4. Use according to any previous claim, wherein the first active ingredient is the R,R enantiomer of formoterol.

5. Use according to any previous claim, wherein a unit dose of formoterol lies in the range of from 1 μg to 48 μg, preferably between 3 μg to 12 μg, calculated as formoterol fumarate dihydrate.

6. Use according to any previous claim, wherein the daily dose of formoterol, including maintenance therapy, lies in the range of from 1 μg to 100 μg, preferably from 2 μg to 60 μg, calculated as formoterol fumarate dihydrate.

7. Use according to any previous claim, wherein the second active ingredient is the 22R epimer of budesonide.

8. Use according to any previous claim, wherein a unit dose of budesonide lies in the range of from 20 µg to 1600 µg, preferably between 50 µg to 400 µg.

9. Use according to any previous claim, wherein the daily dose of budesonide, including maintenance therapy, lies in the range of from 20 µg to 4800 µg, preferably from 30 µg to 3200 µg.

10. Use according to any previous claim, wherein the particle size of the active ingredients (a) and (b) is less than 10 µm.

11. Use according to any previous claim, wherein the composition additionally comprises one or more pharmaceutically acceptable additives, diluents or carriers.

12. Use according to claim 11, wherein the pharmaceutically acceptable additive, diluent or carrier is lactose monohydrate.

13. A method of prevention or treatment of an acute condition of asthma and/or intermittent asthma and/or episodes in chronic asthma, when needed, which comprises administering, by inhalation, to a patient an effective amount of a composition comprising, in admixture:

(a) a first active ingredient which is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and

(b) a second active ingredient which is budesonide.

14. The method according to claim 13, wherein the molar ratio of (a) to (b) calculated as formoterol to budesonide is from 1:1 to 1:100, preferably from 1:1 to 1:70.

15. The method according to claim 13 or 14, wherein the first active ingredient is formoterol fumarate dihydrate.

16. The method according to any of claims 13 to 15, previous claim, wherein the first active ingredient is the R,R enantiomer of formoterol.

17. The method according to any of claims 13 to 16, wherein a unit dose of formoterol lies in the range of from 1 µg to 48 µg, preferably between 3 µg to 12 µg, calculated as formoterol fumarate dihydrate.

18. The method according to any of claims 13 to 17, wherein the daily dose of formoterol, including maintenance therapy, lies in the range of from 1 µg to 100 µg, preferably from 2 µg to 60 µg, calculated as formoterol fumarate dihydrate.

19. The method according to any of claims 13 to 18, wherein the second active ingredient is the 22R epimer of budesonide.

20. The method according to any of claims 13 to 19, wherein a unit dose of budesonide lies in the range of from 20 µg to 1600 µg, preferably between 50 µg to 400 µg.

21. The method according to any of claims 13 to 20, wherein the daily dose of budesonide, including maintenance therapy, lies in the range of from 20 µg to 4800 µg, preferably from 30 µg to 3200 µg.

22. The method according to any of claims 13 to 21, wherein the particle size of the active ingredients (a) and (b) is less than 10 µm.

23. The method according to any of claims 13 to 22, wherein the composition additionally comprises one or more pharmaceutically acceptable additives, diluents or carriers.

24. The method according to claim 23, wherein the pharmaceutically acceptable additive, diluent or carrier is lactose monohydrate.

ABSTRACT

The present invention relates to use of a composition for symptomatic relief, when needed, comprising, in admixture

(a) a first active ingredient which is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and

(b) a second active ingredient which is budesonide;

for the manufacture of a medicament for use in the prevention or treatment of an acute condition of asthma and/or intermittent asthma and/or episodes in chronic asthma. The invention further relates to a method for prevention or treatment of an acute condition of asthma and/or intermittent asthma and/or episodes in chronic asthma by administering, by inhalation, a composition comprising the first and second active ingredients as defined previously.

PATENT

ATTORNEY DOCKET NO: 06275/188001

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled NEW USE, the specification of which

☐ is attached hereto.
☐ was filed on as Application Serial No.
and was amended on (if applicable).

☒ was described and claimed in PCT International Application No. SE99/01031 filed on 10 June 1999 and was amended under PCT Article 19 on (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose all information I know to be material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

COUNTRY	APPLICATION NO.	FILING DATE	PRIORITY CLAIMED
Sweden	9802073-8	11 June 1998	☒Yes ☐ No

I hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Janis K. Fraser, Reg. No. 34,819; William E. Booth, Reg. No. 28,933; John W. Freeman, Reg. No. 29,066; J. Peter Fasse, Reg. No. 32,983; Timothy A. French, Reg. No. 30,175; Eldora L. Ellison, Reg. No. 39,967; John J. Gagel, Reg. No. 33,499; John F. Hayden, Reg. No. 37,640.

Address all telephone calls to Janis K. Fraser, Esq. at telephone number 617/542-5070.

Address all correspondence to Janis K. Fraser, Esq., Fish & Richardson P.C., 225 Franklin Street, Boston, MA 02110-2804.

I hereby authorize the attorneys and/or agents named above to accept and follow instructions from my

COMBINED DECLARATION AND POWER OF ATTORNEY CONTINUED

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Full Name of Inventor: Tommy Ekström

Inventor's Signature: _____ Date: 15 June 1995

Residence Address: ~~Linköping~~, Sweden

Citizen of: Sweden

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